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Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience

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(Article begins on next page)

# Surgical Endoscopy

## Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience

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<b>Order of Authors Secondary Information:</b>	
<b>Author Comments:</b>	<p>Rome, November 27, 2018</p> <p>To the attention of the Editorial Office of Surgical Endoscopy Cover letter of the paper: "Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience"</p> <p>The present retrospective study is submitted to your attention for review and possibly for publication in Surgical Endoscopy. The manuscript has not been previously published and is not under consideration for publication in any other journal. This is the first reported series of patients who underwent laparoscopic bilateral adrenalectomy (LBA) via a transperitoneal anterior approach. For this reason, despite the limited sample size, we consider that this paper might be of interest for the readers of the journal due to several advantages that are associated with the anterior approach in bilateral adrenalectomy cases in comparison to the lateral and retroperitoneal routes.</p> <p>All authors have read and approved the manuscript and its submission to the journal. Looking forward to receiving your reply, I remain</p> <p>Sincerely,</p>

	<p>Andrea Balla, MD, (Corresponding author)          Department of General Surgery and Surgical Specialties "Paride Stefanini", Sapienza University of Rome, Italy          Azienda Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome, Italy          Telephone number: +39.339.4746893          Fax: +39.06.49970549          e-mail: andrea.balla@gmail.com</p>
<p><b>Response to Reviewers:</b></p>	<p>Professor George B. Hanna          Editor-in-Chief          Surgical Endoscopy</p> <p>Dear Professor Hanna,</p> <p>We wish to thank you for having accepted the manuscript entitled "Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience" for publication. The manuscript has been revised according to the comments made by the reviewers. All comments have been addressed and changes have been made and highlighted in the manuscript, as follows:</p> <p>#Reviewer 1:</p> <p>1.This manuscript is a review of 21 patients who underwent laparoscopic adrenalectomy via an anterior transperitoneal approach. It provides additional insights regarding surgical approaches but would be greatly enhanced by intraoperative photos of port placement and intraabdominal views (both left and right). The authors should also consider a more robust discussion of limitations of this approach and of their experience; have they attempted any cortical sparing adrenalectomies with this approach and is the view limited at all? what were the outcomes of these approaches?</p> <p>•Seven intraoperative photos were added in the manuscript. Unfortunately, we do not have experience with the cortical sparing adrenalectomy and this was mentioned in the Discussion as follows: "The authors, however, have no experience with this procedure. Although it seems a valuable treatment strategy, larger patient samples are required to reach definitive conclusions.          Our approach also has some technical limitations. In some obese patients undergoing right adrenalectomy the liver made heavy and fragile from steatosis occasionally may require a second 5 mm. retractor introduced from an extra right subcostal trocar. During left adrenalectomy the operative field is usually narrow, its boundaries being initially the inferior mesenteric vein medially and the left ascending colic vessels laterally; subsequently and in a more posterior plane the boundaries of the operative field become the body of the pancreas and the splenic vein above, the renal vein below, the aorta medially and the spleen laterally. Recognition of these anatomical landmarks is straightforward. However, gentle dissection along avascular planes is mandatory to avoid blood filling up the narrow operative field and obscuring vision."</p> <p>#Reviewer 2:</p> <p>1.This clever piece of research does present a novel series structure. The text is clear concise. Results are clear and endpoint easily identified. The data is sequestered from the series previously presented more than once. That is why it offers little clinical benefit as far as clinical data is concerned. Also the cases are performed over many years during which surgeon experience, technology, anesthesia and drugs have all dramatically changed. This has its effect on the "homogeneity" of the study sample.</p> <p>•The long period of our experience, as a limitation of the study, has been included in the Discussion as follows: "Moreover, the long time span of our experience could have affected the homogeneity of the study sample."</p> <p>The revised manuscript is now submitted to your attention for publication in Surgical Endoscopy.</p> <p>Looking forward to receiving your reply, I remain</p>

	<p>Sincerely,</p> <p>Andrea Balla, MD,  Department of General Surgery and Surgical Specialties “Paride Stefanini”, Sapienza University of Rome, Italy  andrea.balla@gmail.com</p>
<b>Funding Information:</b>	
<b>Abstract:</b>	<p>Background: The aim of this study is to evaluate the feasibility, safety, advantages and surgical outcomes of laparoscopic bilateral adrenalectomy (LBA) by an anterior transperitoneal approach.</p> <p>Methods: From 1994 to 2018, 552 patients underwent laparoscopic adrenalectomy, unilateral in 531 and bilateral in 21 patients (9 females and 12 males). All patients who underwent LBA were approached via a transperitoneal anterior route, and form our study population. Indications included: Cushing’s disease (n=11), pheochromocytoma (n=6), Conn’s disease (n=3) and adrenal cysts (n=1).</p> <p>Results: Mean operative time was 195 ± 86.2 minutes (range 55 – 360 minutes). Conversion was necessary in one case for bleeding. Three patients underwent concurrent laparoscopic cholecystectomy with laparoscopic common bile duct exploration and ductal stone extraction in one. Three postoperative complications occurred in one patient each: subhepatic fluid collection, intestinal ileus and pleural effusion. Mean hospital stay was 6.1 ± 4.7 days (range 2 – 18 days).</p> <p>Conclusions: In our experience transperitoneal anterior LBA was feasible and safe. Based on our results we believe that this approach leads to prompt recognition of anatomical landmarks with early division of the main adrenal vein prior to any gland manipulation, with a low risk of bleeding and without the need to change patient position. Unlike the lateral approach, there is no need to mobilize the spleno-pancreatic complex on the left or the liver on the right. The ability to perform associated intraperitoneal procedures, if required, is an added benefit.</p>

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# Laparoscopic bilateral anterior transperitoneal adrenalectomy: 24 years experience

**Running head:** Laparoscopic bilateral anterior adrenalectomy

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## ABSTRACT

**Background:** The aim of this study is to evaluate the feasibility, safety, advantages and surgical outcomes of laparoscopic bilateral adrenalectomy (LBA) by an anterior transperitoneal approach.

**Methods:** From 1994 to 2018, 552 patients underwent laparoscopic adrenalectomy, unilateral in 531 and bilateral in 21 patients (9 females and 12 males). All patients who underwent LBA were approached via a transperitoneal anterior route and form our study population. Indications included: Cushing's disease (n=11), pheochromocytoma (n=6), Conn's disease (n=3) and adrenal cysts (n=1).

**Results:** Mean operative time was  $195 \pm 86.2$  minutes (range 55 – 360 minutes). Conversion was necessary in one case for bleeding. Three patients underwent concurrent laparoscopic cholecystectomy with laparoscopic common bile duct exploration and ductal stone extraction in one. Three postoperative complications occurred in one patient each: subhepatic fluid collection, intestinal ileus and pleural effusion. Mean hospital stay was  $6.1 \pm 4.7$  days (range 2 – 18 days).

**Conclusions:** In our experience transperitoneal anterior LBA was feasible and safe. Based on our results we believe that this approach leads to prompt recognition of anatomical landmarks with early division of the main adrenal vein prior to any gland manipulation, with a low risk of bleeding and without the need to change patient position. Unlike the lateral approach, there is no need to mobilize the spleno-pancreatic complex on the left or the liver on the right. The ability to perform associated intraperitoneal procedures, if required, is an added benefit.

**Key words:** Laparoscopic bilateral adrenalectomy (LBA); Laparoscopic transperitoneal anterior adrenalectomy; Laparoscopic transperitoneal anterior submesocolic left adrenalectomy

## INTRODUCTION

1  
2 Minimally invasive adrenalectomy has become the gold standard [1-7] since Gagner's first  
3  
4 laparoscopic unilateral adrenalectomy in lateral decubitus [2]. Afterwards other approaches have  
5  
6 been proposed, including the retroperitoneal with the patient in the prone or lateral decubitus  
7  
8 position, the anterior transperitoneal with colonic flexure mobilization and the left submesocolic [6-  
9  
10 9]. As of today, no formal superiority of one mini-invasive approach over another has emerged for  
11  
12 uni- or laparoscopic bilateral adrenalectomy (LBA) [1-7].  
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16  
17 Bilateral adrenalectomy is performed less often than unilateral adrenalectomy [8]: according  
18  
19 to the British Association of Endocrine and Thyroid Surgeons only 6% of patients undergoing  
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21 adrenal gland surgery underwent bilateral adrenalectomy in 2012 [1]. The indications for bilateral  
22  
23 adrenalectomy, include adrenocorticotrophic hormone (ACTH) dependent hypercortisolism  
24  
25 (Cushing's or Conn's disease), hereditary pheochromocytoma [Multiple Endocrine Neoplasia 2 a-b  
26  
27 (MEN2), Von Hippel Lindau (VHL) disease] [1] and life-threatening conditions such as patients with  
28  
29 ectopic Cushing's syndrome due to metastatic disease or ACTH secreting pituitary macroadenomas  
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31 [9,10].  
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37 The aim is to report our 24 year experience with LBA via an anterior transperitoneal  
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39 approach evaluating its feasibility, safety, advantages and surgical outcomes.  
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## MATERIALS AND METHODS

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45 This study is a retrospective analysis of prospectively collected data, approved by our  
46  
47 Institutional review board. Informed consent was obtained from all participants.  
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52 From January 1994 to August 2018, 552 patients underwent surgery for adrenal gland  
53  
54 disease in two centers (Department of General Surgery and Surgical Specialties "Paride Stefanini",  
55  
56 Sapienza University of Rome and Department of General Surgery, Università Politecnica delle  
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58 Marche, Ancona, Italy) that followed the same treatment protocol and used an identical surgical  
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60 approach [3-6]. Out of 552 patients, 531 patients (96.2%) underwent unilateral adrenalectomy and  
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1 the remaining 21 patients (3.8%) underwent anterior transperitoneal LBA and form our study  
2 population. These included nine women and twelve men, mean age  $41.9 \pm 12.1$  years (range 21 - 67  
3 years) with mean BMI of  $28.1 \pm 3.9$  Kg/m<sup>2</sup> (range 21 - 37 Kg/m<sup>2</sup>). One patient had undergone a  
4 previous appendectomy (Table 1).  
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9 Preoperatively, all patients had full endocrinological evaluation including laboratory and  
10 imaging tests. Indications for surgery were: Cushing's disease (n=11), pheochromocytoma (n=6),  
11 Conn's disease (n=3), large adrenal cysts (n=1).  
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16 After surgery, all patients received substitutive therapy according to local policies.  
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## 21 **Surgical technique**

22 Similar to our surgical techniques for unilateral right and left adrenalectomy described  
23 previously [3-6], candidates for LBA are positioned supine with abducted legs, a 12-13 mmHg  
24 pneumoperitoneum is created with a Veress needle and optical trocar above the umbilicus or with  
25 an open technique and Hasson cannula, under general anesthesia. A 30° or 45° forward oblique  
26 optic is inserted [3-6]. The operating table is in slight anti-Trendelenburg position and with the side  
27 opposite the lesion tilted down. The surgeon stands in between the patient's legs for the left side and  
28 ipsilateral to the lesion for the right side.  
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41 Six trocars are employed (Figure 1): two on the midline, one 12 mm, 2-3 centimeters above  
42 the umbilicus (n. 1), and one 5 mm, below the xiphoid process (n. 2) used for exposure on both  
43 sides. Two trocars are placed on the right, one 12 mm (n. 3) at the junction between the right  
44 anterior axillary line and the transverse umbilical line and one 5 mm (n. 4) along the right  
45 midaxillary line (Figure 1). Two 12 mm trocars are placed on the left, one at the junction of the left  
46 midclavicular line with the transverse umbilical line (n. 5) and the other along the left anterior  
47 axillary line (n. 6) (Figure 1). The optic is alternatively introduced in trocars n. 3 and 5, while  
48 trocars 1 - 4 and 1 - 6 are used for the manipulation instruments, on the right and on the left,  
49 respectively.  
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1 Right adrenalectomy is performed by a direct anterior transperitoneal approach while left  
2 anterior adrenalectomy requires opening the root of the left transverse mesocolon to reach the gland  
3 behind the pancreas [3-6].  
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7 Right adrenalectomy starts by dividing any adhesion between the gallbladder, greater  
8 omentum and transverse colon in order to lift the right liver with a Nathanson retractor (Cook  
9 Medical, Bloomington, Indiana, USA) or Endo Paddle retractor (Covidien, Mansfield,  
10 Massachusetts, USA) introduced from trocar n. 2, so as to expose Morrison's pouch. The posterior  
11 parietal peritoneum is then opened longitudinally along the right margin of the inferior vena cava  
12 above the duodenum (Figure 2), and the main adrenal vein is identified and divided between clips  
13 (Figure 3) [3-6].  
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24 For left adrenalectomy, the transverse mesocolon is retracted cephalad by atraumatic forceps  
25 introduced from trocar n. 2, in order to identify the arch of the inferior mesenteric vein and to  
26 expose the ligament of Treitz after displacing the first jejunal loop to the right of the patient (Figure  
27 4). The posterior parietal peritoneum is then opened over the lower border of the pancreas at the  
28 root of the transverse mesocolon, between the first jejunal loop and the inferior mesenteric vein. In  
29 some cases, depending on the individual patient anatomy, the peritoneum may be opened lateral to  
30 the inferior mesenteric vein, if this is closer to the first jejunal loop. By blunt and sharp dissection,  
31 Toldt's fascia is opened and the retro-pancreatic space is entered after raising the body of the  
32 pancreas. Gerota's fascia is then incised and the left renal vein is identified. Its superior margin is  
33 followed medially until the inferior adrenal vein is identified, prepared and divided between clips  
34 (Figure 5 and 6) [3-6].  
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51 Care is taken to avoid any manipulation of the adrenal gland prior to division of the main  
52 adrenal vein in both right and left adrenalectomy. Surgical dissection is performed with a bipolar  
53 diathermy (LigaSure™ tissue fusion, Covidien, Mansfield, Massachusetts, USA) or ultrasonic  
54 (Ultracision, Harmonic Scalpel, Ethicon Endo Surgery, Cincinnati, Ohio, USA) device. The adrenal  
55 vein is divided between titanium (AcuClip, Tyco / Healthcare, Norwalk, Connecticut, USA) or Hem-  
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1 o-lok (Weck® Hem-o-lok®, Teleflex, North Carolina, USA) clips. Once fully mobilized, the gland is  
2 removed with a specimen retrieval bag (Inzii® Retrieval Systems, Applied Medical, Rancho Santa  
3 Margarita, California, USA). The residual adrenal cavities are routinely filled with hemostatic  
4 facilitators (Flo seal, Baxter Healthcare Corporation, Deerfield, Illinois, USA or Surgiflo Hemostatic  
5 Matrix Kit, Ethicon Endo-Surgery, Johnson & Johnson, Cincinnati, Ohio, USA) (Figures 7 and 8).  
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7 Drains are placed in the right and/or left adrenal fossae, based on surgeon's preference [3-6].  
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### 17 **Study data**

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19 We recorded gender, age, body mass index (BMI), previous abdominal surgery, operative  
20 time, associated procedures, conversions, postoperative complications (graded according to the  
21 Clavien-Dindo classification [11]), blood transfusions, hospital stay, size of specimen and definitive  
22 histology. These were collected in a Microsoft Excel program (Microsoft Corporation, Redmond,  
23 Washington, USA).  
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### 34 **Analysis**

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36 Results are expressed as mean  $\pm$  standard deviation (SD) for continuous variables and  
37 percentages for categorical variables. No statistical tests were used because of the small numbers.  
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## 43 **RESULTS**

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46 Mean operative time was  $195 \pm 86.2$  minutes (range 55 – 360 minutes). Conversion to open  
47 surgery was necessary in one case for bleeding and required postoperative blood transfusions (grade  
48 II according to Clavien-Dindo classification [11]).  
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54 Three patients underwent concomitant laparoscopic cholecystectomy (LC), which was  
55 associated with laparoscopic common bile duct exploration (LCBDE), stones extraction and T-tube  
56 placement in one case.  
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1 Postoperative complications were observed in three patients: subhepatic fluid collection in  
2 the gallbladder bed (Clavien-Dindo grade II) after concurrent cholecystectomy during LBA for  
3 pheochromocytoma, intestinal ileus (Clavien-Dindo grade I) and pleural effusion (Clavien-Dindo  
4 grade I) in one patient each after LBA for Cushing syndrome. Mean hospital stay was  $6.1 \pm 4.7$   
5 days (range 2 - 19 days). Oral intake was possible on postoperative day one in all patients having an  
6 uneventful postoperative course. There were no deaths.  
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14 Mean adrenal gland size was  $3 \pm 2.1$  cm (range 0.7 - 9.3 cm) and  $3.1 \pm 2.1$  cm (range 0.5 -  
15 6.6 cm) for right and left glands, respectively. Definitive histology was: adrenal hyperplasia (n=14),  
16 pheochromocytoma (n=6) and adrenal cysts (n=1).  
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## 24 **DISCUSSION**

25  
26 In the authors' experience laparoscopic anterior transperitoneal bilateral adrenalectomy was  
27 feasible, safe and effective; only one conversion was necessary, three patients had grade I-II  
28 morbidity and no mortality. All patients were cured of their disease.  
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34 Of note, two of 11 patients with Cushing disease had grade I morbidity. This is of interest as  
35 Cushing's syndrome is reported to be associated with a higher frequency of postoperative  
36 complications, including an increased risk of thromboembolism [12].  
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41 There are four available access options for mini-invasive adrenalectomy- the transperitoneal  
42 lateral and anterior, retroperitoneal lateral and posterior routes [7] - with no clear superiority of one  
43 approach over another [7].  
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48 The SAGES guidelines state: "Several approaches to laparoscopic adrenalectomy have been  
49 described in the literature. Surgeons should choose the approach they are most familiar with, have  
50 had training in, and have the best patient outcomes with (+++, strong recommendation)." [7]. The  
51 lateral transperitoneal and the retroperitoneal approaches are the most popular, probably because  
52 they are perceived to be advantageous (larger exposition and direct approach, respectively) by some  
53 surgeons [3-6].  
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1 The anterior transperitoneal approach for bilateral adrenalectomy has been our preference  
2 for the last two decades [3-6,13,14]. In open surgery, the submesocolic approach to left  
3 adrenalectomy was first proposed by Pierre Delbet, a French surgeon, in 1912 [15] whereas in  
4 laparoscopy, this approach was first reported as case reports by Sardi (1994) and Robertson (1995)  
5 [16,17]. In our opinion the anterior approach provides unparalleled vision and recognition of the  
6 anatomy. It allows secure control and division of the adrenal vein at the beginning of the procedure  
7 prior to any gland manipulation, thereby reducing the risk of bleeding and avoiding any hormone  
8 release. Should accidental major bleeding occur, it allows quick conversion to open surgery without  
9 the need to change patient position. During left adrenalectomy by the submesocolic technique,  
10 neither mobilization of the splenic flexure of the colon nor of the spleno-pancreatic complex is  
11 required to obtain gland exposure, unlike the transperitoneal lateral approach [3-6]. This should  
12 reduce the risk of organ damage, postoperative wandering spleen with potential acute gastric  
13 volvulus and left pneumothorax [4,5,18-21]. During right adrenalectomy there is no need for liver  
14 mobilization, thereby reducing the risk of bleeding from accessory hepatic veins, and early division  
15 of the right adrenal vein before any gland mobilization makes the procedure safer because it  
16 increases the working distance between the gland and the inferior vena cava [3-6]. During bilateral  
17 adrenalectomy, both the anterior transperitoneal and the posterior retroperitoneal approach allow to  
18 complete the operation without repositioning the patient on the operative table [1,22-27]. In the  
19 authors' opinion, this is a remarkable advantage compared to the lateral approach because it saves  
20 time. The possibility to perform associated procedures, if necessary, without the need to reposition  
21 the patient on the operative table [3-6] is perceived by the authors as an additional benefit.

22 In the literature there are only few reports on LBA [1,22-31], the most popular approach also  
23 being lateral (Table 2) [1,22-31]. Comparing our operative outcomes with those in the literature, it  
24 seems that the operative time is shorter as compared to the lateral approach, while the conversion  
25 and morbidity rates are similar (Table 2) [1,22-31]. Patient samples in some of the reported series,

1 however, were small and overall surgical approaches were heterogeneous, sometimes multiple  
2 and/or in two stages (Table 2) [1,22-31].  
3

4 As substitutive therapy is mandatory after complete bilateral adrenalectomy, a more  
5 conservative surgical approach for the treatment of Cushing's syndrome, including a unilateral  
6 adrenalectomy and a partial contralateral adrenalectomy, has also been reported [32]. Lowery *et al.*  
7 reported their experience with this approach, showing encouraging results in terms of operative  
8 time, conversion and complication rates, without the need for lifelong steroid therapy [32]. The  
9 authors, however, have no experience with this procedure. Although it seems a valuable treatment  
10 strategy, larger patient samples are required to reach definitive conclusions.  
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21 Our approach also has some technical limitations. In some obese patients undergoing right  
22 adrenalectomy the liver made heavy and fragile from steatosis occasionally may require a second 5  
23 mm. retractor introduced from an extra right subcostal trocar. During left adrenalectomy the  
24 operative field is usually narrow, its boundaries being initially the inferior mesenteric vein medially  
25 and the left ascending colic vessels laterally; subsequently and in a more posterior plane the  
26 boundaries of the operative field become the body of the pancreas and the splenic vein above, the  
27 renal vein below, the aorta medially and the spleen laterally. Recognition of these anatomical  
28 landmarks is straightforward. However, gentle dissection along avascular planes is mandatory to  
29 avoid blood filling up the narrow operative field and obscuring vision.  
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43 The limitations of the present study are its two center, same single team, retrospective  
44 nature, the lack of a control group and of a group of patients who underwent cortical sparing  
45 adrenalectomy as well as the relatively small sample size. Moreover, the long time span of our  
46 experience could have affected the homogeneity of the study sample.  
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53 To the best of authors' knowledge, however, this is the first reported series of patients  
54 undergoing laparoscopic bilateral adrenalectomy by an anterior approach.  
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58 LBA with transperitoneal anterior and submesocolic approaches has proven to be feasible  
59 and safe. Relevant technical features of this procedure are early division of the adrenal vein as the  
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1 first step of the procedure prior to any gland manipulation, which is important to enhance the safety  
2 of the procedure, and the fact that there is no need to mobilize the colonic flexure and the spleno-  
3 pancreatic complex on the left, no need to mobilize the liver on the right, reducing the extent of  
4 dissection and the surgical risk. The transperitoneal anterior approach with the patient supine allows  
5 the surgeon to perform bilateral adrenalectomy and associated intraperitoneal procedures without  
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**DISCLOSURES**

1  
2 Dr. Andrea Balla, Dr. Monica Ortenzi, Dr. Livia Palmieri, Dr. Diletta Corallino, Dr. Francesca  
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4 Meoli, Dr. Pietro Ursi, Dr. Giulia Puliani, Dr. Emilia Sbardella, Prof. Andrea M. Isidori, Prof.  
5  
6 Mario Guerrieri, Dr. Silvia Quaresima and Prof. Alessandro M. Paganini declare that they have no  
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9 conflict of interest or financial ties to disclose.  
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## REFERENCES

1. Maccora D, Walls GV, Sadler GP, Mihai R. (2017). Bilateral adrenalectomy: a review of 10 years' experience. *Ann R Coll Surg Engl.* Feb;99(2):119-122. doi: 10.1308/rcsann.2016.0266.
2. Gagner M. (1996). Laparoscopic adrenalectomy. *Surg Clin North Am.* Jun;76(3):523-37.
3. Scoglio D, Balla A, Paci M, Guerrieri M, Lezoche G, D'Ambrosio G, Fabiani B, Ursi P, Paganini AM. (2013). Laparoscopic transperitoneal anterior adrenalectomy. *Ann Ital Chir.* Jul-Aug;84(4):411-6.
4. Paganini AM, Balla A, Guerrieri M, Lezoche G, Campagnacci R, D'Ambrosio G, Quaresima S, Antonica MV, Lezoche E. (2014). Laparoscopic transperitoneal anterior adrenalectomy in pheochromocytoma: experience in 62 patients. *Surg Endosc.* Sep;28(9):2683-9. doi: 10.1007/s00464-014-3528-4.
5. Paganini AM, Guerrieri M, Balla A, Quaresima S, Isidori AM, Iafrate F, D'Ambrosio G, Lezoche G, Lezoche E. (2016). Management of adrenal incidentaloma by laparoscopic transperitoneal anterior and submesocolic approach. *Langenbecks Arch Surg.* Feb;401(1):71-9. doi: 10.1007/s00423-015-1367-y.
6. Balla A, Quaresima S, Palmieri L, Ortenzi M, Sbardella E, Puliani G, Isidori AM, Guerrieri M, Paganini AM. (2018). Is laparoscopic left adrenalectomy with the anterior submesocolic approach for Conn's or Cushing's syndrome equally safe and effective as the lateral and anterior ones? *Surg Endosc.* Nov 19. doi:10.1007/s00464-018-6601-6.
7. Stefanidis D, Goldfarb M, Kercher KW, Hope WW, Richardson W, Fanelli RD; Society of Gastrointestinal and Endoscopic Surgeons. (2013). SAGES guidelines for minimally invasive treatment of adrenal pathology. *Surg Endosc.* Nov;27(11):3960-80. doi: 10.1007/s00464-013-3169-z.
8. Park HS, Roman SA, Sosa JA. (2009). Outcomes from 3144 adrenalectomies in the United States: which matters more, surgeon volume or specialty? *Arch Surg.* Nov;144(11):1060-7. doi: 10.1001/archsurg.2009.191.
9. Pivonello R, Isidori AM, De Martino MC, Newell-Price J, Biller BM, Colao A. (2016). Complications of Cushing's syndrome: state of the art. *Lancet Diabetes Endocrinol.* Jul;4(7):611-29. doi: 10.1016/S2213-8587(16)00086-3.
10. Pozza C, Graziadio C, Giannetta E, Lenzi A, Isidori AM. (2012). Management Strategies for Aggressive Cushing's Syndrome: From Macroadenomas to Ectopics. *J Oncol.* 2012:685213. doi: 10.1155/2012/685213.
11. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. (2009). The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg.* Aug;250(2):187-96.
12. Isidori AM, Minnetti M, Sbardella E, Graziadio C, Grossman AB. (2015). Mechanism in endocrinology: The spectrum of haemostatic abnormalities in glucocorticoid excess and defect. *Eur J Endocrinol.* Sep;173(3):R101-13. doi: 10.1530/EJE-15-0308.
13. Lezoche E, Guerrieri M, Crosta F, Lezoche G, Baldarelli M, Campagnacci R. (2008). Flank approach versus anterior sub-mesocolic access in left laparoscopic adrenalectomy: a prospective randomized study. *Surg Endosc.* Nov;22(11):2373-8. doi: 10.1007/s00464-008-9783-5.

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14. Lezoche E, Guerrieri M, Feliciotti F, Paganini AM, Perretta S, Baldarelli M, Bonjer J, Miccoli P. (2002). Anterior, lateral, and posterior retroperitoneal approaches in endoscopic adrenalectomy. *Surg Endosc.* Jan;16(1):96-9.
15. Benedetti-Valentini S, Rossodivita I. (1968). Delbet's submesocolic approach for surgery of the left adrenal gland. *Osp Ital Chir.* Mar;18(3):285-8.
16. Sardi A, McKinnon WM. (1994). Laparoscopic adrenalectomy in patients with primary aldosteronism. *Surg Laparosc Endosc.* Apr;4(2):86-91.
17. Robertson CS, Chung SC, Bouchier-Hayes D, Cockram CS, Li AK. (1995). Laparoscopic left adrenalectomy: a new approach. *Aust N Z J Surg.* Aug;65(8):619-20.
18. Col V, de Canniere L, Collard E, Michel L, Donckier J. (1999). Laparoscopic adrenalectomy for pheochromocytoma: endocrinological assessment. *Clin Endocrinol (Oxf)* 50:121-5.
19. Corcione F, Tricarico F, Barbaros U, Marzano E, Montini F, Trombetti A. (2008). Gastric volvulus after laparoscopic left adrenalectomy: case report. *Surg Laparosc Endosc Percutan Tech.* Apr;18(2):207-8. doi: 10.1097/SLE.0b013e318169ce4f.
20. Piccoli M, De Luca GM, Pasculli A, Angelini M, Guicciardi L, Mullineris B, Marchi D, Melotti G. (2014). Laparoscopic transperitoneal left adrenalectomy and wandering spleen risk. *JLS.* Jul-Sep;18(3). pii: e2014.00278. doi: 10.4293/JLS.2014.00278.
21. Henry JF, Defechereux T, Raffaelli M, Lubrano D, Gramatica L. (2000). Complications of laparoscopic adrenalectomy: results of 169 consecutive procedures. *World J Surg.* Nov;24(11):1342-6.
22. Aggarwal S, Yadav K, Sharma AP, Sethi V. (2013). Laparoscopic bilateral adrenalectomy for Cushing syndrome: surgical challenge lessons learnt. *Surg Laparosc Endosc Percutan Tech.* Jun;23(3):324-8. doi: 10.1097/SLE.0b013e318290126d.
23. Lan BY, Taskin HE, Aksoy E, Birsen O, Dural C, Mitchell J, Siperstein A, Berber E. (2015). Factors affecting the surgical approach and timing of bilateral adrenalectomy. *Surg Endosc.* Jul;29(7):1741-5. doi: 10.1007/s00464-014-3891-1.
24. Gilbert EW, Harrison VL, Sheppard BC. (2014). The adrenal psoas sign: surgical outcomes following a simple technique to maximize removal of extracortical adrenal tissue during bilateral laparoscopic adrenalectomy. *Surg Endosc.* Sep;28(9):2666-70. doi: 10.1007/s00464-014-3524-8.
25. Takata MC, Kebebew E, Clark OH, Duh QY. (2008). Laparoscopic bilateral adrenalectomy: results for 30 consecutive cases. *Surg Endosc.* Jan;22(1):202-7.
26. Vella A, Thompson GB, Grant CS, van Heerden JA, Farley DR, Young WF Jr. (2001). Laparoscopic adrenalectomy for adrenocorticotropin-dependent Cushing's syndrome. *J Clin Endocrinol Metab.* Apr;86(4):1596-9.
27. Hawn MT, Cook D, Deveney C, Sheppard BC. (2002). Quality of life after laparoscopic bilateral adrenalectomy for Cushing's disease. *Surgery.* Dec;132(6):1064-8; discussion 1068-9.
28. Porpiglia F, Fiori C, Bovio S, Destefanis P, Alì A, Terrone C, Fontana D, Scarpa RM, Tempia A, Terzolo M. (2004). Bilateral adrenalectomy for Cushing's syndrome: a comparison between laparoscopy and open surgery. *J Endocrinol Invest.* Jul-Aug;27(7):654-8.
29. Miccoli P, Materazzi G, Brauckhoff M, Ambrosini CE, Miccoli M, Dralle H. (2011). No outcome differences between a laparoscopic and retroperitoneoscopic approach in synchronous bilateral adrenal surgery. *World J Surg.* Dec;35(12):2698-702. doi: 10.1007/s00268-011-1294-1.

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- 30. Raffaelli M, Brunaud L, De Crea C, Hoche G, Oragano L, Bresler L, Bellantone R, Lombardi CP. (2014). Synchronous bilateral adrenalectomy for Cushing’s syndrome: laparoscopic versus posterior retroperitoneoscopic versus robotic approach. *World J Surg.* Mar;38(3):709-15. doi: 10.1007/s00268-013-2326-9.
- 31. Pugliese R, Boniardi M, de Carli S, Sansonna F, Costanzi A, Maggioni D, Ferrari GC, Di Lernia S, Loli P, Grossrubatscher E. (2008). Laparoscopic bilateral simultaneous adrenalectomy: results of 11 operations. *J Laparoendosc Adv Surg Tech A.* Aug;18(4):588-92. doi: 10.1089/lap.2007.0116.
- 32. Lowery AJ, Seeliger B, Alesina PF, Walz MK. (2017). Posterior retroperitoneoscopic adrenal surgery for clinical and subclinical Cushing’s syndrome in patients with bilateral adrenal disease. *Langenbecks Arch Surg.* Aug;402(5):775-785. doi: 10.1007/s00423-017-1569-6.

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3 **Figure 1.** Trocar positions for laparoscopic transperitoneal anterior bilateral adrenalectomy.

4 **Figure 2.** Right adrenalectomy: the posterior peritoneum prior to longitudinal division along the  
5 right margin of the inferior vena cava. The peritoneal division is then extended cranially towards the  
6 diaphragm.

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9 **Figure 3.** Right adrenalectomy: the right adrenal vein has been identified and divided between  
10 clips. The adrenal gland is located underneath the grasper.

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13 **Figure 4.** Left adrenalectomy: the arch of the inferior mesenteric vein is identified at the level of the  
14 duodeno-jejunal angle exposing the posterior peritoneum at the insertion of the transverse  
15 mesocolon along the inferior margin of the pancreas.

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19 **Figure 5.** Left adrenalectomy: the inferior adrenal vein has been identified. The left adrenal gland is  
20 visible but no manipulation of the gland has yet occurred.

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23 **Figure 6.** Left adrenalectomy: the inferior adrenal vein has been closed with clips prior to its  
24 division.

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27 **Figure 7.** Right adrenalectomy: the residual cavity immediately prior to its being filled with  
28 hemostatic facilitators.

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31 **Figure 8.** Left adrenalectomy: the residual cavity immediately prior to its being filled with  
32 hemostatic facilitators.

**Table 1. Results.**

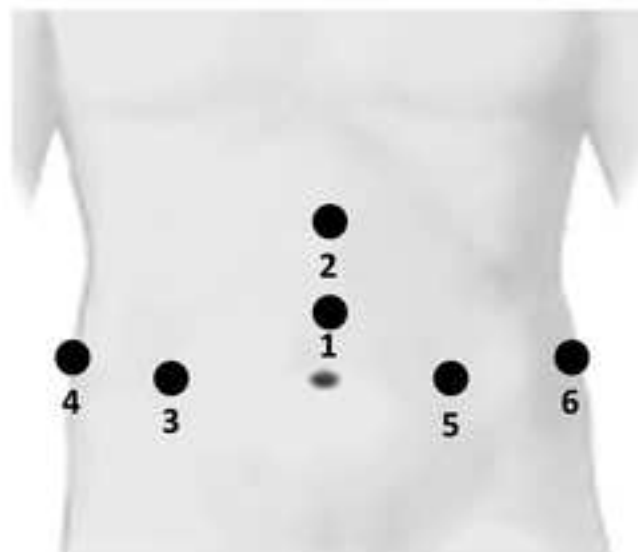
<b>Sex ratio (F/M)</b>	9/12
<b>Mean age <math>\pm</math> SD, years (range)</b>	41.9 $\pm$ 12.1 (21 – 67)
<b>Mean BMI <math>\pm</math> SD, Kg/m<sup>2</sup> (range)</b>	28.1 $\pm$ 3.9 (21 - 37)
<b>Previous abdominal surgery, n</b>	1
<b>Mean operative time <math>\pm</math> SD, minutes (range)</b>	195.0 $\pm$ 86.2 (55 - 360)
<b>Associated procedures, n</b>	3
- Cholecystectomy	2
- Cholecystectomy + LCBDE	1
<b>Conversions, n</b>	1
<b>Complications, n (Clavien-Dindo classification, grade)</b>	3 (2 II, 1 I)
<b>Blood transfusions in patients, n</b>	1
<b>Mean hospital stay <math>\pm</math> SD, days (range)</b>	6.1 $\pm$ 4.7 (2 – 19)
<b>Mean adrenal gland size <math>\pm</math> SD, cm (range)</b>	
- Right	3 $\pm$ 2.1 (0.7 – 9.3)
- Left	3.1 $\pm$ 2.1 (0.5 – 6.6)
<b>Definitive histology, n</b>	
- Adrenal hyperplasia	14
- Pheochromocytoma	6
- Adrenal cysts	1

**SD: standard deviation. LCBDE: laparoscopic common bile duct exploration.**

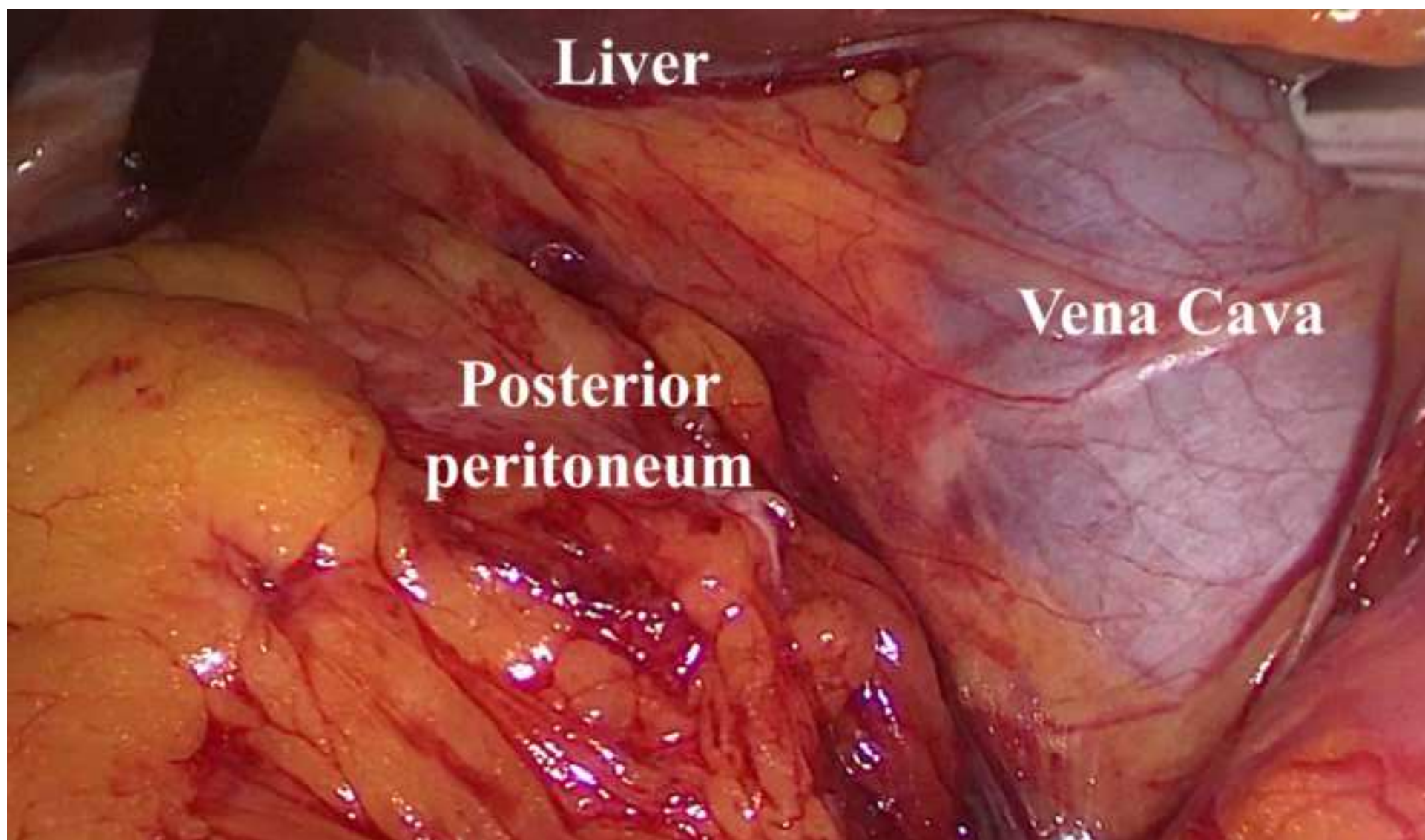
**Table 2. Patient series of laparoscopic bilateral adrenalectomy reported in the literature.**

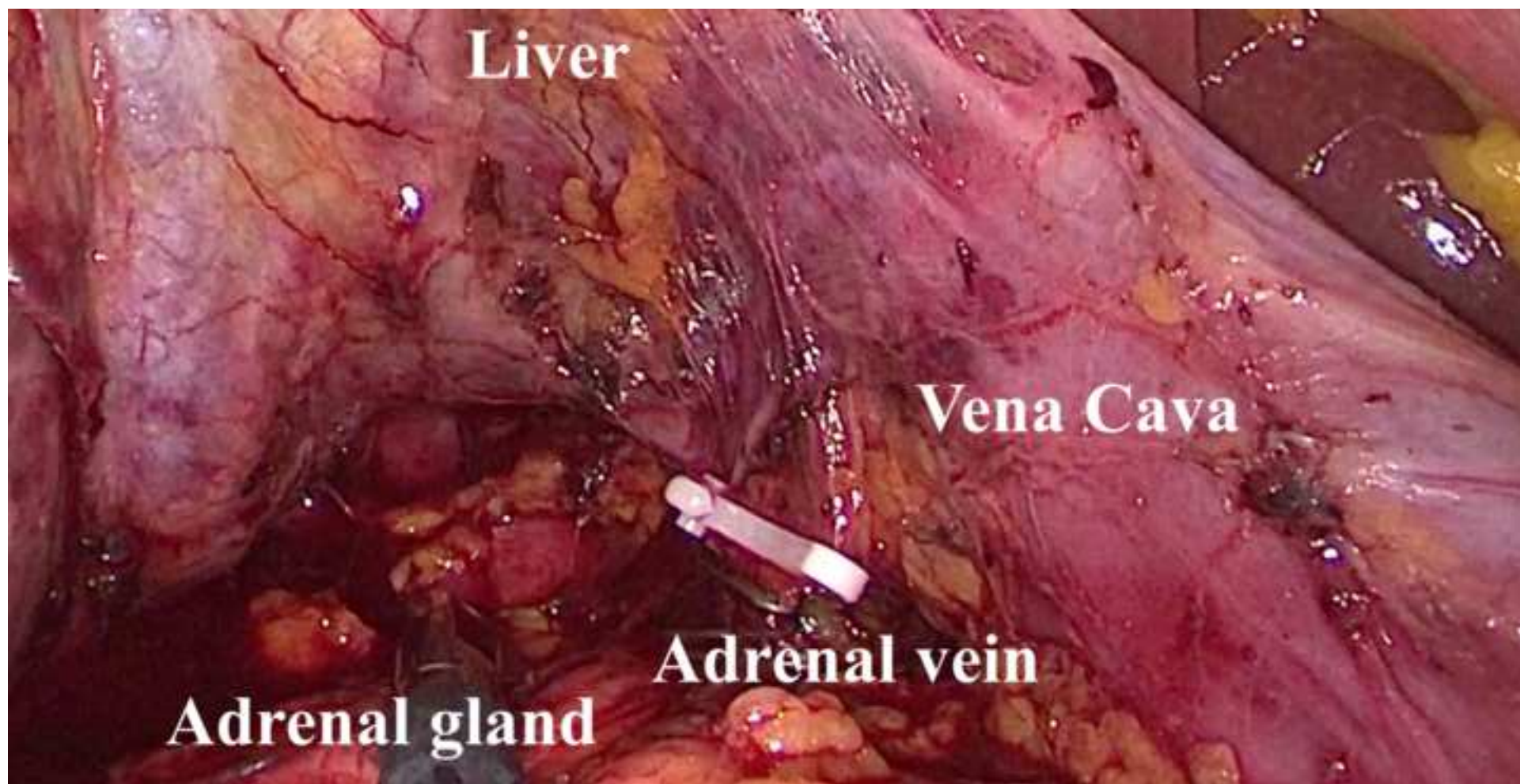
Authors	Number of patients	Approach	Mean age $\pm$ SD (years)	Mean operative time $\pm$ SD or range (minutes)	Conversion, n	Intra - postoperative complications, n	Mean hospital stay $\pm$ SD or range (days)	Mortality, n
Maccora [1]	17 3 3	Lateral Posterior Open	43 $\pm$ 4	195 $\pm$ 16 151 $\pm$ 12 243 $\pm$ 44	1 - -	8	8.8	1
Aggarwal [22]	15 one stage 4 two stage	Lateral	25.4	210 (150-240) -	- -	3	n.r.	1
Lan [23]	9 * 17 °	Lateral Posterior	54.9 $\pm$ 14.3 59.7 $\pm$ 17.7	374 $\pm$ 157 334 $\pm$ 93	- -	2 2	3.5 $\pm$ 2.1 2.7	- -
Gilbert [24]	92	Lateral	40	272 $\pm$ 79.2	2	3	n.r.	1
Takata [25]	30	Lateral	44	290 (180 - 480)	-	6	3.5 (1 - 12)	-
Vella [26]	19	Lateral	n.r.	252 (160 - 360)	3	-	2.7 (2 - 5)	-
Hawn [27]	18	Lateral	47 (18 - 72)	296 (160 - 420)	-	3	3 (1 - 18)	-
Porpiglia [28]	13	Lateral	47.2 $\pm$ 13	234 $\pm$ 39	2	1	5.7 $\pm$ 0.9	-
Miccoli [29]	20 14	Lateral Posterior	48.1 38.9	180.6 170	2 1	- -	5.25 8.2	- -
Raffaelli [30]	5 11 13	Lateral Posterior Lateral rob	46.8 $\pm$ 19.9 41.2 $\pm$ 13.1 42.8 $\pm$ 13.6	256.0 $\pm$ 43.4 157.4 $\pm$ 54.6 221.5 $\pm$ 42.2	- 1 -	0 4 5	12 $\pm$ 5.7 10.8 $\pm$ 3.7 4.4 $\pm$ 1.7	- - -
Pugliese [31]	7 3 1	Lateral Posterior Combined	45.6 $\pm$ 17.8	245 $\pm$ 41.3 218 $\pm$ 22 405	- - -	2	5 $\pm$ 1.8	-
Present series	21	Anterior	41.9 $\pm$ 12.1	195.0 $\pm$ 86.2	1	3	6.1 $\pm$ 4.7	-

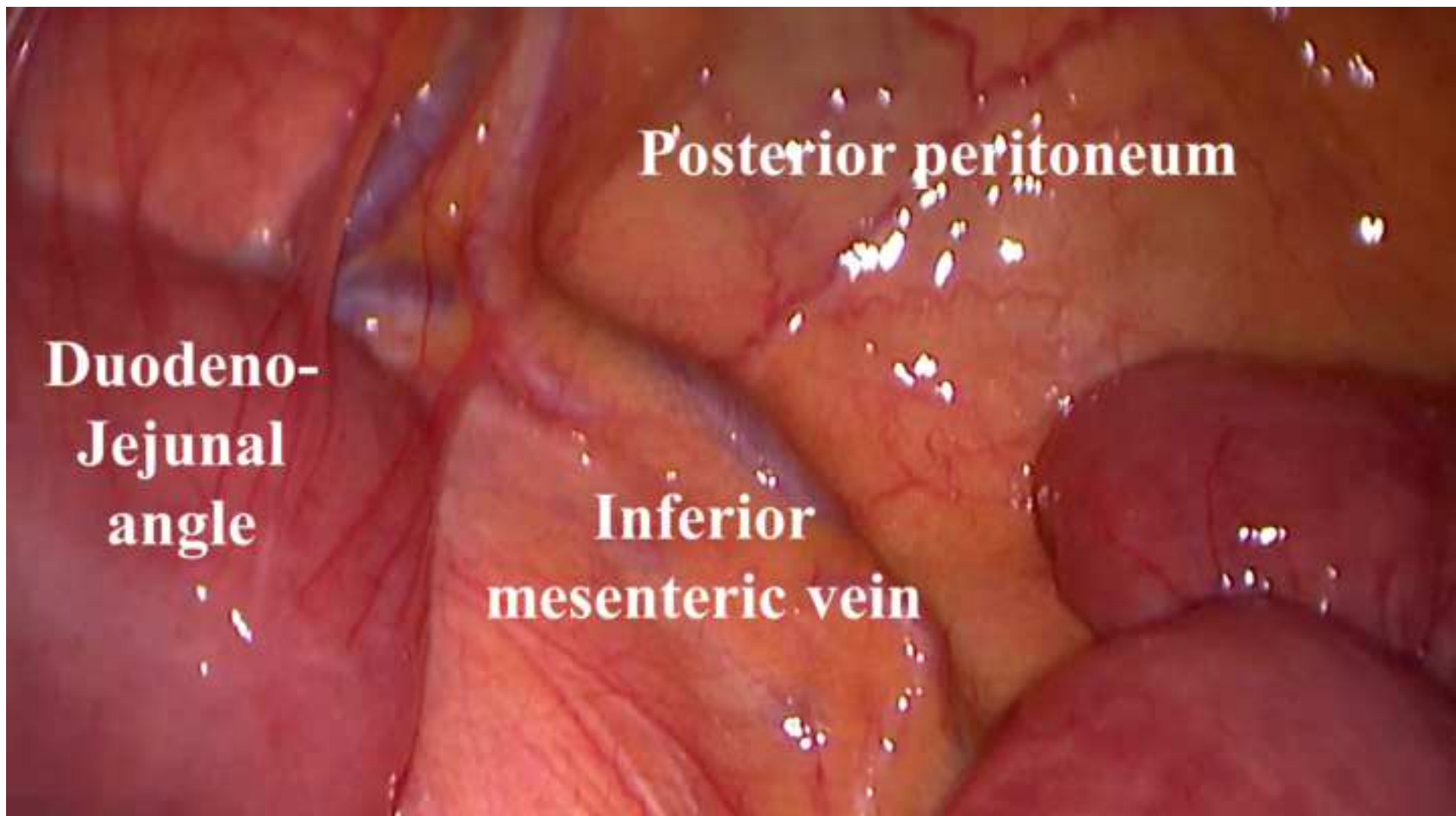
SD: standard deviation. \*: two patients underwent two stage adrenalectomy. °: one patient underwent two stage adrenalectomy. n.r.: not reported. Rob: robotic.

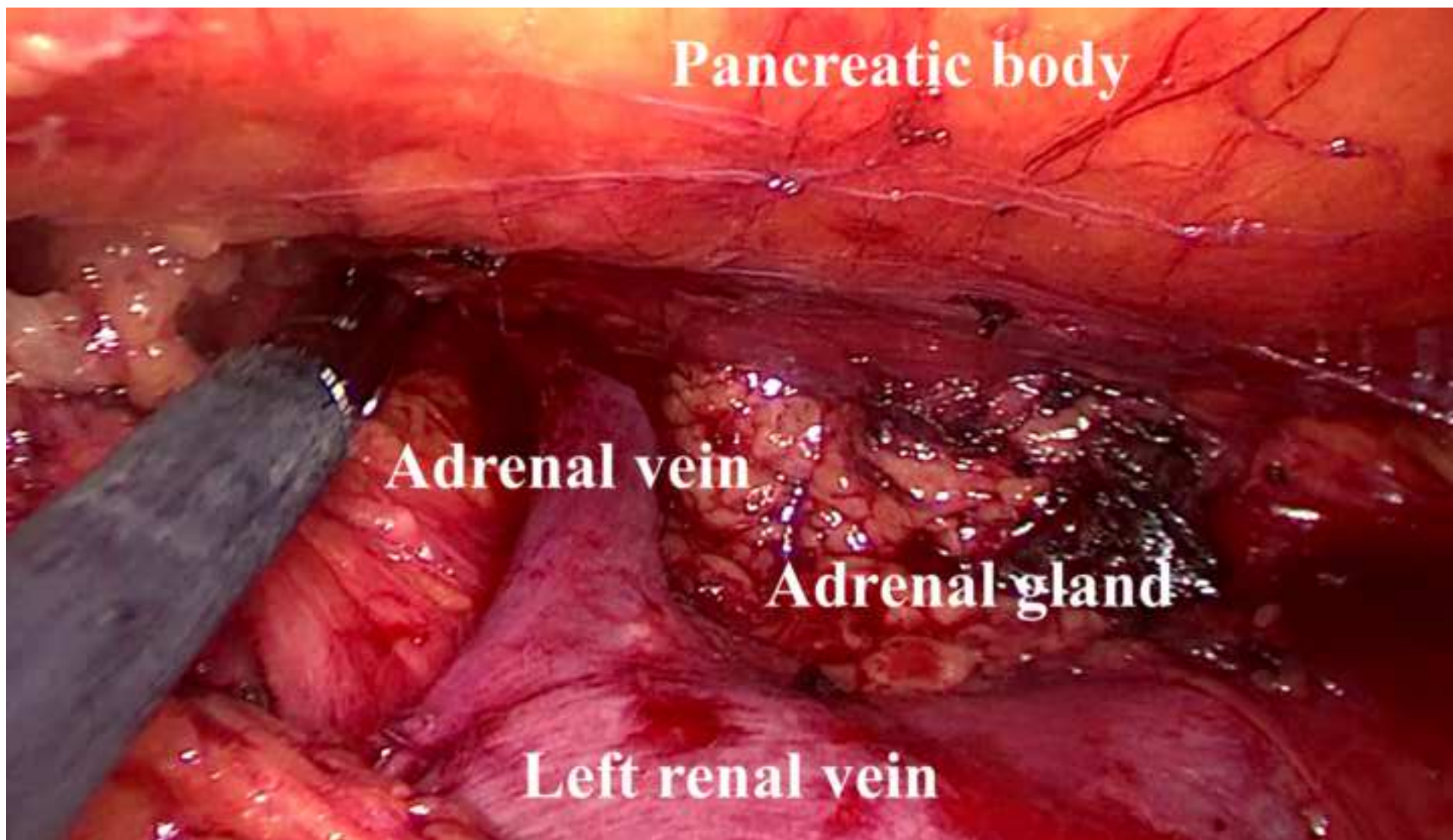


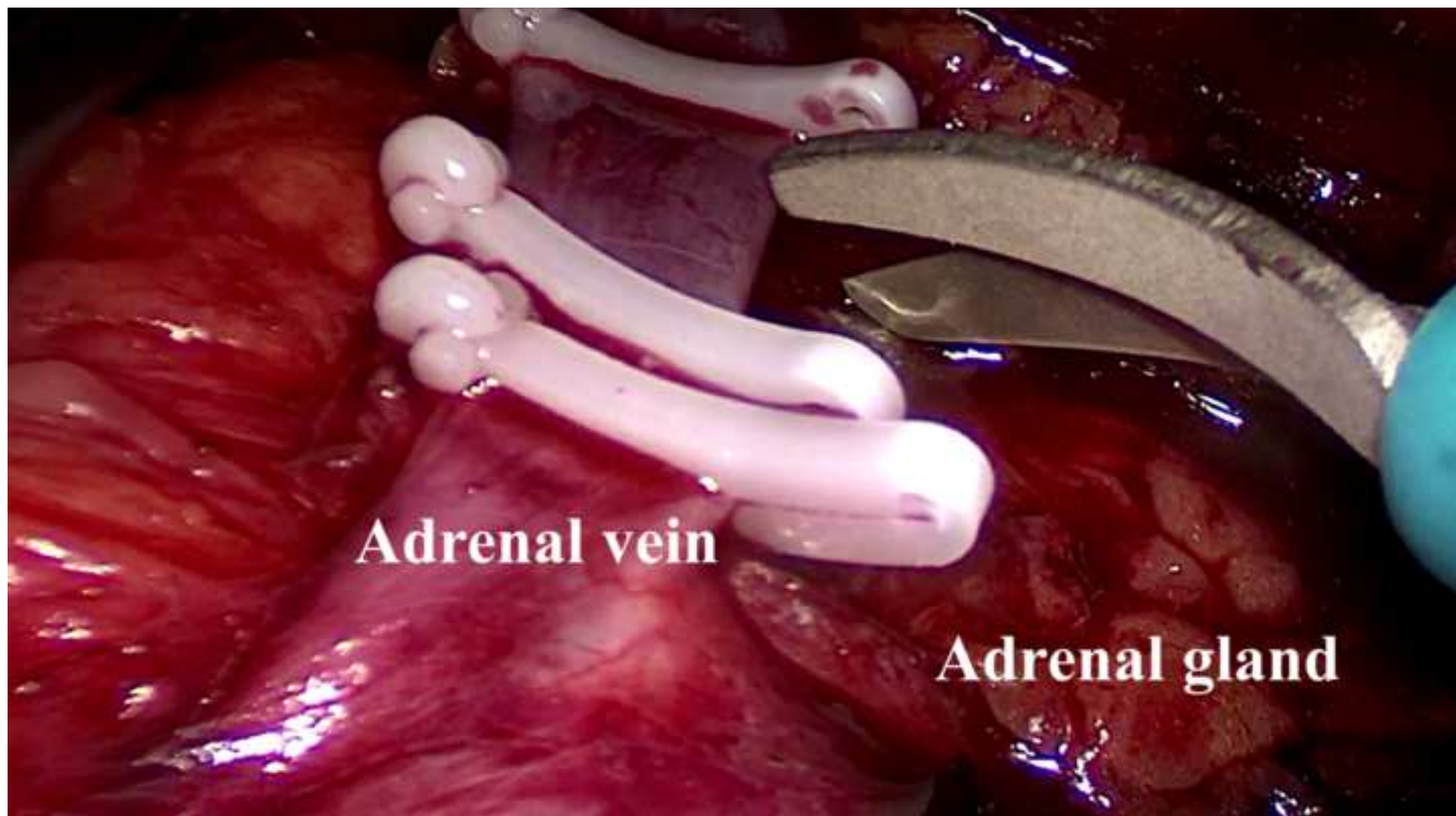


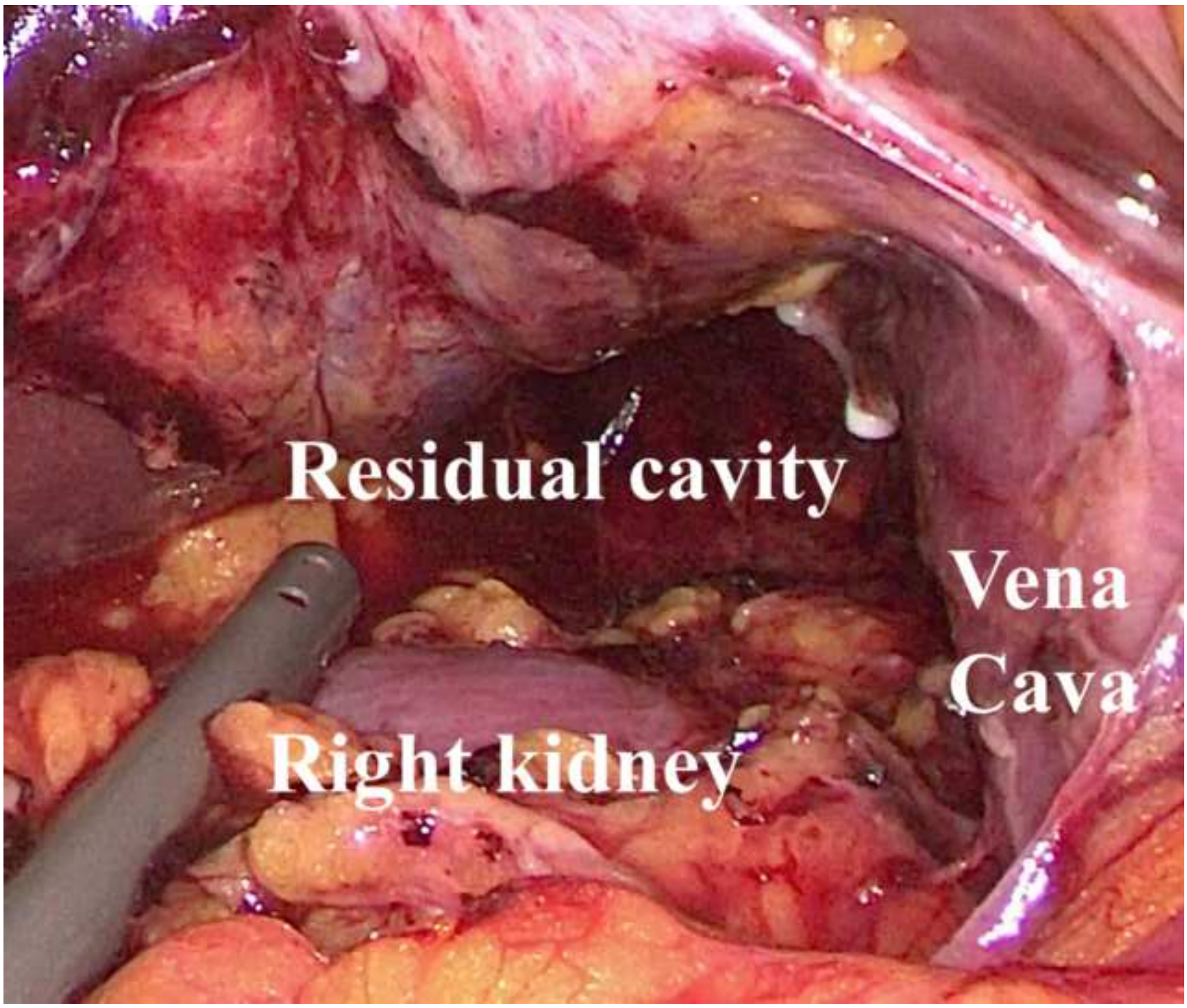








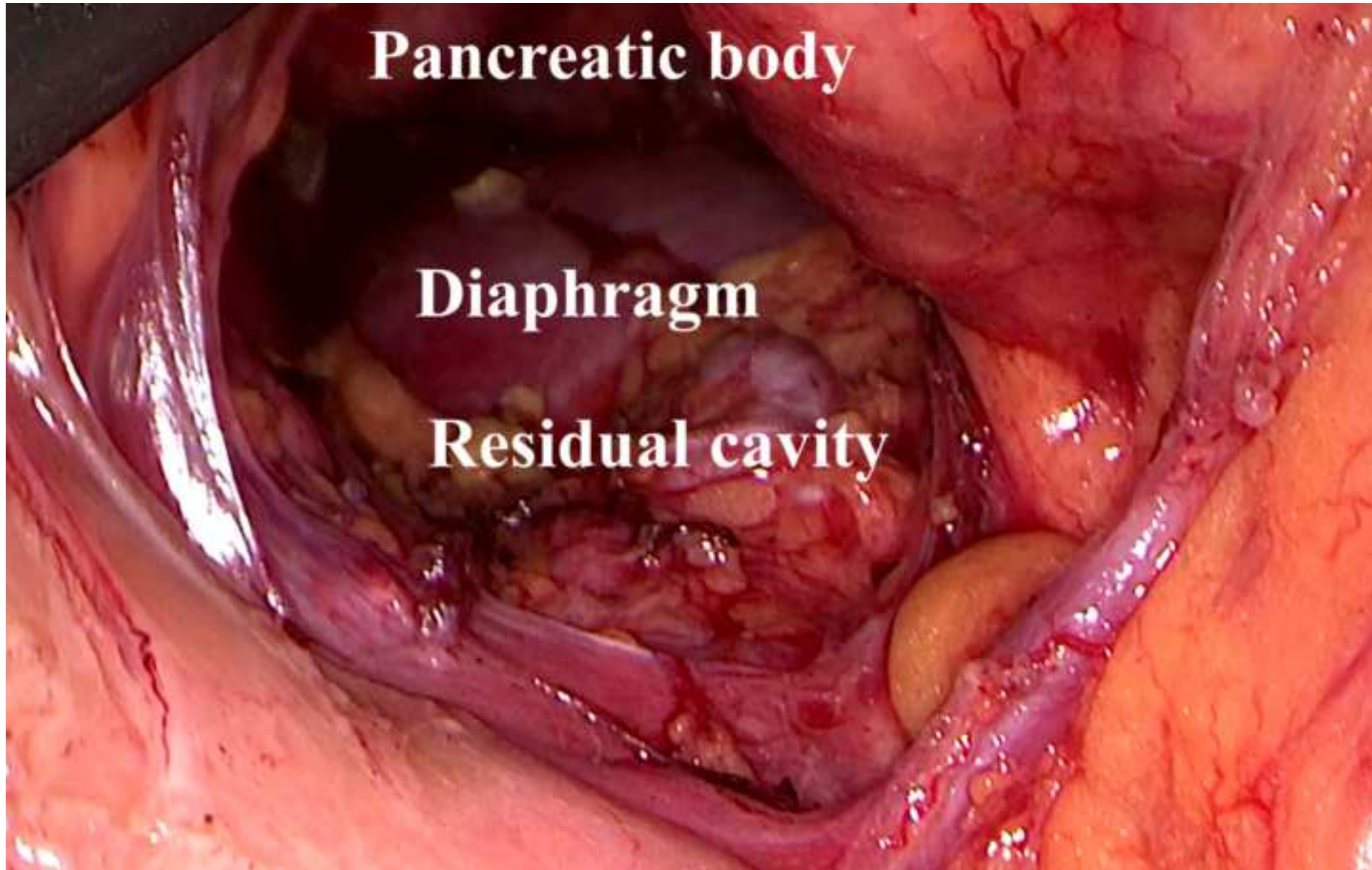




**Residual cavity**

**Vena  
Cava**

**Right kidney**



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